13 Genotype, disease severity, and healthcare resource use by patients with CF in the UK National Health Service

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Background: The clinical manifestations of CF can be wide-ranging and often require a variety of treatments administered by multi-disciplinary teams. Long-term management of CF is related to disease severity and complications and impacts the costs associated with treatment of CF.
Objective: To describe clinical characteristics and evaluate resource use in clinical practice by CF genotype.
Methods: A retrospective chart review of 200 patients (pts) ⩾6 years of age with CF and the G551D/other or ΔF508/ΔF508 mutation (genotypes that represent nearly 60% of UK pts) selected from four adult and four paediatric CF centres was performed. Each centre contributed 25 pts, including all G551D/other pts and randomly-selected ΔF508/ΔF508 pts. For each pt, the most recent two years of eligible, uninterrupted resource use and clinical data were collected. Data from June 2007 to March 2012 were used.
Results: See Tables.
Conclusion: These pts with CF had a pattern of high resource use, including multiple hospitalizations and the administration of polypharmacy. Resource use was similar across G551D/other and ΔF508/ΔF508 genotypes, despite some differences in clinical characteristics.

Patient characteristics at initial data point

	Age Mean (SD)	Gender % Female	FEV_1% Mean (SD)	% PA culture positive	% Pancreatic insufficient	Nutrition (Wt/age z score) Mean (SD)	% CFRD positive
G551D/other (n = 63)	23.5 (11.8)	48	64.6 (22.7)	54	90	0.33 (1.1)	13
ΔF508/ΔF508 (n = 137)	17.7 (9.4)	50	69.4 (24.3)	49	96	–0.21 (1.0)	16

Healthcare utilization over two years

	Routine Visits Mean (SD)	No. of Hospns Mean (SD)	Total No. of Hosp days Mean (SD)	Hosp IV days Mean (SD)	Home IV days Mean (SD)	Neb AB n (%)	Dornase n (%)
G551D/other (pts, n = 63)	14.0 (8.4)	3.4 (3.4)	49 (82)	35 (40)	45 (80)	55 (87)	42 (67)
ΔF508/ΔF508 (pts, n = 137)	15.7 (9.3)	3.5 (3.3)	48 (84)	39 (46)	33 (49)	119 (87)	98 (72)

14 Genetic characterization of the pediatric patients from southern and central Portugal and islands

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Objectives: To characterize the population of patients with cystic fibrosis followed at pediatric centers on the central and southern regions of Portugal and islands (Azores and Madeira).
Methods: Collection of data from the data bases of all the cystic fibrosis pediatric centers in these regions. Patients in follow-up during 2012 were included.
Conclusion and Results: 139 patients (pts) were identified: 62 (44.6%) males, 2 with less than 1 year (y), 6 aged 1–2 y, 11 aged 3–5 y, 41 aged 6–10 y and 79 older than 11 y. F508del mutation is the commonest one: 77 pts (55.4%) homozygous and 62 (44.6%) heterozygous. Other more common mutations found are: G542X (4.8% of the alleles), A561E (3.8%), R1066C and R334W (2.7% each) and N1303K (2.2%).
Age of diagnosis varied between prenatal and 16 y: 67 pts were diagnosed under 1 y of age, 24 at 1–2 y, 13 at 3–5 y, 20 at 6–10 y and 8 older than 11 y. This last group includes 2 pts f508 homozygous.
Comments: Only 6 mutations have been found in more than 1 or 2 pts. Several pts, including some with classic mutations, have been diagnosed at a late age. Neonatal screening could lead to a significantly earlier diagnosis in this population.

15 Update of CFTR mutation frequencies in cystic fibrosis patients in Uruguay

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In June 2010, the First National Reference Center for Diagnosis and Treatment of Patients with Cystic Fibrosis was created. An algorithm for mandatory newborn screening was incorporated: an inmuno-reactive trypsin test (IRT/IRT) on dried blood spot followed by a by sweat test and molecular analysis.
Aim: To assess a genotyping, and to calculate the frequencies of mutation distribution in a population of probable or confirmed CF patients.
Methods: From 2010 to 2012, blood samples were processed either coming from newborn screening or from patients attending the CF Reference Center. Additionally we analyzed the frequency of the mutation in 100 unrelated DF508 healthy controls. Genomic DNA was extracted from peripheral blood lymphocytes, by Qiagen Dneasy Blood and Tissue kit. The panel was chosen based on the known mutations of patients diagnosed at that time. The selected panel covered over 95% of the mutations found ethnic added to epidemiology.
Results: Of the 126 DNA analyzed we found that only 60 had two (48.3%) or one (51.7%) of the mutations sought. The most frequent allele was DF508 (42.5%), followed by G542X (5.8%) and R334W (5.0%). The N1303K, W1282X, R1162X, 2183AA>G, 3120+1G>A, 1078delT, R117H and 5T alleles appeared with a frequency less than 2.5%.
Conclusions: We could achieve a mutational diagnosis in only the 23% of patients. This could be due to false positive diagnosed CF patients or the mutational panel was not the appropriated one. In the patients identified by the screening protocol and diagnosed by a positive sweat test, without or with only one mutation, a complete CFTR sequencing will be performed.

16 The −765G>C and 8473T>C polymorphism in *COX2* gene and 57460C>T polymorphism in *IFRD1* gene as modifiers of cystic fibrosis severity

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Objectives: To verify the association between the −765G>C and 8473T>C polymorphism in *COX2* gene and 57460C>T polymorphism in *IFRD1* gene with the Cystic Fibrosis (CF) severity.
Methods: 103 patients were included, 55 were female and 97 Caucasians. Clinical variables: sex, race, scores [Shwachman-Kulczycki, Kanga and Bhalla], BMI, patient age, age at diagnosis, initial symptoms (digestive and pulmonary), first colonization by *Pseudomonas aeruginosa,* microorganisms [*P. aeruginosa* and mucoid non-mucoid, *Achromobacter xylosoxidans* (AX), *Staphylococcus aureus*, *Burkolderia cepacia* (BC)], SaO2, spirometry and comorbidities [nasal polyps, osteoporosis, meconium ileus (MI), pancreatic insufficiency, diabetes mellitus (DM)]. Statistical analysis was performed using SPSS v.17.0, Open Epi v.5.0 and the R version 2.12. Data were compared by different tests according to the data distribution. Data were compared using chi square test and Fisher exact test. For all analyzes, we adopted alpha = 0.05. The CFTR mutations were used in the analysis in association with the polymorphisms. There was not found association, except for meconium ileus ($p = 0.028$ – in patients with two *CFTR* mutations from class I, II and III) and for nasal polyposis ($p = 0.022$ – in patients whose *CFTR* genotype was not considered) to the 8473T>C polymorphism in COX2 gene with *odds ratio* of 5.552 (95 IC: 1.318–38.27) and 5.486 (95 IC: 1.192–40) to CC + GC, respectively.
Conclusion: The 8473T>C polymorphism in the COX2 gene is a possible modifier gene of CF.